

Sonographically Guided Core Needle Biopsy of Cervical Lymphadenopathy in Patients Without Known Malignancy

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Objective. The purpose of this study was to retrospectively evaluate the efficacy of sonographically guided core needle biopsy (core biopsy) for diagnosing the causes of cervical lymphadenopathy in patients without known malignancy. **Methods.** One hundred fifty-five sonographically guided core biopsies performed in 155 patients with cervical lymphadenopathy were retrospectively evaluated. None of the 155 patients had any known primary malignancy. Final diagnoses were determined by the histologic examination from excision biopsy when performed or by the clinical and sonographic follow-up for more than 12 months. When a lymph node diagnosed as benign by sonographically guided core biopsy regressed spontaneously or by subsequent management, the diagnosis made by the sonographically guided core biopsy was considered correct. When a lymph node diagnosed as benign by sonographically guided core biopsy was unchanged or increased in size with subsequent management, excision biopsy was performed. Diagnostic yield, sensitivity, specificity, accuracy, and complications of core biopsy were evaluated. **Results.** Histologic diagnosis could be made by sonographically guided core biopsy in 146 (94%) of the 155 patients. The histologic diagnoses were reactive hyperplasia in 44 patients, tuberculosis in 37, Kikuchi disease in 25, metastasis in 16, lymphoma in 16, normal in 7, and toxoplasmosis in 1. Sensitivity, specificity, and accuracy of sonographically guided core biopsy were 97.9%, 99.1%, and 97.9%, respectively. There were no procedure-related complications. **Conclusions.** Sonographically guided core biopsy is a safe and efficient tool for diagnosing the cause of cervical lymphadenopathy in patients without known malignancy and may obviate unnecessary excisional biopsy. **Key words:** core biopsy; lymph node; neck mass; sonography.

Abbreviations

FNAC, fine-needle aspiration cytologic examination

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Cervical lymphadenopathy can arise either from benign or from malignant causes. For assessment of cervical lymphadenopathy, fine-needle aspiration cytologic examination (FNAC) is widely used. The reported diagnostic accuracy of FNAC in malignant lymphadenopathy ranges from 79% to 94.5%,¹⁻³ but limitations of FNAC include a high rate of nondiagnostic sampling, a high rate of false-negative diagnoses in Hodgkin disease, and incomplete classification of non-Hodgkin lymphoma.^{4,5} When FNAC for unexplained cervical lymphadenopathy results in a nondiagnostic or an equivocal report, excision biopsy may be required. However, excision biopsy requires hospital admission, at times may need general anesthesia, and may even result in adverse outcomes.⁶

Sonographically guided core needle biopsy (core biopsy) provides a larger tissue sample that retains its architecture and permits the use of a range of histochemical and immunohistochemical staining. Therefore, a more precise histologic assessment can be made to diagnose the causes of cervical lymphadenopathy. A few studies reported that sonographically guided core biopsy in assessment of cervical lymphadenopathy was a safe and accurate procedure in differentiating benign causes from malignancies.^{7,8}

The purpose of this study was to retrospectively evaluate the efficacy of sonographically guided core biopsy for diagnosing the causes of cervical lymphadenopathy in patients without known malignancy.

Materials and Methods

The Institutional Review Board approved this retrospective study, and informed consent was not required. The results of 155 consecutive sonographically guided core biopsies performed in 155 patients between March 2000 and September 2005 were retrospectively evaluated. The patients' ages ranged from 13 to 82 years (mean, 38 years). All biopsies were performed as part of an evaluation of patients with unexplained cervical lymphadenopathy for 1 to 6 months. Inclusion criteria for sonographically guided core biopsy were as follows: (1) unexplained cervical lymphadenopathy either on physical examination or on an imaging study for more than 1 month, (2) no known malignancy, and (3) a short diameter of the lymph node of 1.0 cm or greater. Sonographic morphologic criteria regarding a benign or malignant appearance were not used for determination of the necessity for core biopsy. Platelet counts and coagulation times were not routinely checked. None of the patients were premedicated. All sonographically guided core biopsies were performed by 1 of the 2 staff radiologists on an outpatient basis.

Sonographic evaluation of the neck was performed with a 7.5- to 10-MHz linear array transducer (HDI 5000; Philips Medical Systems, Bothell, WA). A color Doppler study was routinely used to identify the location of intervening vessels. For core biopsy, the probe was covered with sterilized vinyl. The skin was sterilized with povi-

done-iodide, which was also used as an acoustic couplant. After local anesthesia with 1% lidocaine, a tiny incision was made on the skin. Core biopsy was performed under sonographic guidance by a freehand technique (Figure 1) with a disposable 16-gauge single-action automatic core biopsy needle (Pro-Mag 2.2; Manan Medical Products, Northbrook, IL) or a 16-gauge dual-action semiautomatic core biopsy needle (Stericut; TSK Laboratory, Tochigi, Japan). The throw of both biopsy needles used was 2.2 cm. Core biopsy was repeated until an adequate amount of specimen was obtained on visual inspection. We used a 16-gauge core biopsy needle instead of an 18-gauge core biopsy needle for acquisition of a larger tissue sample. After each biopsy, the site and size of the lymph node and the number of biopsies were recorded. When present, procedure-related complications were also recorded. The patient was instructed to compress the biopsy site manually for 30 minutes and was reexamined by sonography. If no complication was detected, the patient was discharged without any medication.

Tissue cores were stained with hematoxylin-eosin, and, if needed, additional histochemical and immunohistochemical stains were added. Histologic diagnoses for the sonographically guided core biopsies were reported as definitive, suggestive but not definitive, or nondiagnostic. The final diagnoses were determined by the results of histologic examination from excision biopsy when performed or by the clinical course and sonographic follow-up for more than 12 months. When a lymph node diagnosed as benign by sonographically guided core biopsy regressed spontaneously or by subsequent management, the diagnosis made by the sonographically guided core biopsy was considered correct. When a lymph node diagnosed as benign by sonographically guided core biopsy was unchanged or increased in size with subsequent management, excision biopsy was performed.

The diagnostic yield, sensitivity, specificity, accuracy, and complications of sonographically guided core biopsy were evaluated with standard methods using an Excel 2000 version 9.0 spreadsheet (Microsoft Corporation, Redmond, WS). The sonographically guided core biopsies were

analyzed in 2 populations: (1) a population that included all 155 biopsy results in which nondiagnostic and suggestive results were considered incorrect and (2) a population in which nondiagnostic results were excluded and suggestive diagnoses were regarded as incorrect diagnoses.

Results

The number of biopsies per patient ranged from 2 to 4 (mean, 2.5) biopsies. The location of the lymph nodes sampled were in level I in 4 patients, level II in 21, level III in 14, level IV in 22, and level V in 80. The precise location was not recorded for 14 biopsies. The short diameter of the nodes sampled ranged from 1.0 to 7 cm (mean, 2.8 cm).

Histologic diagnosis could be made by sonographically guided core biopsy in 146 (94%) of the 155 patients. Table 1 details the histologic diagnoses made by sonographically guided core biopsy. In the 146 patients with histologic results, histologic diagnoses were definitive in 144 patients and were highly suggestive in 2. The 2 highly suggestive results were Hodgkin lymphoma and tuberculosis, which were confirmed as Hodgkin lymphoma and tuberculous lymphadenitis in the subsequent excision biopsies, respectively. Nondiagnostic results were reported in 9 patients. Seven biopsies were due to inadequate amounts of tissue specimen, and 2 biopsies were reported to be fibroadipose tissue only. Subsequent excision biopsies were performed in 7 of the 9 patients. The results of excision biopsy for the 7 patients were follicular lymphoma in 1 patient, tuberculous lymphadenitis in 2, and reactive hyperplasia in 4. In the 2 patients who had no excision biopsy, the cervical lymphadenopathies resolved spontaneously within 1 month and were considered benign.

Table 2 lists the histologic diagnoses of malignant lymphadenopathy and their confirmed primary cancers or classification of lymphoma at excision biopsies in the 146 sonographically guided core biopsies. Among the 16 patients with metastatic lymphadenopathy diagnosed by sonographically guided core biopsy, primary cancers were found through workup after core biopsy in 14 patients. The histologic type of the

Figure 1. Sonograms during core needle biopsy using a dual-action semiautomatic core biopsy needle. **A**, Prefiring sonogram shows the guiding needle placed at the target (arrows). **B**, The needle position before firing shows accurate placement of the sample notch within the lesion (arrows). **C**, After firing, the outer blade advances over the cutting notch (arrows).

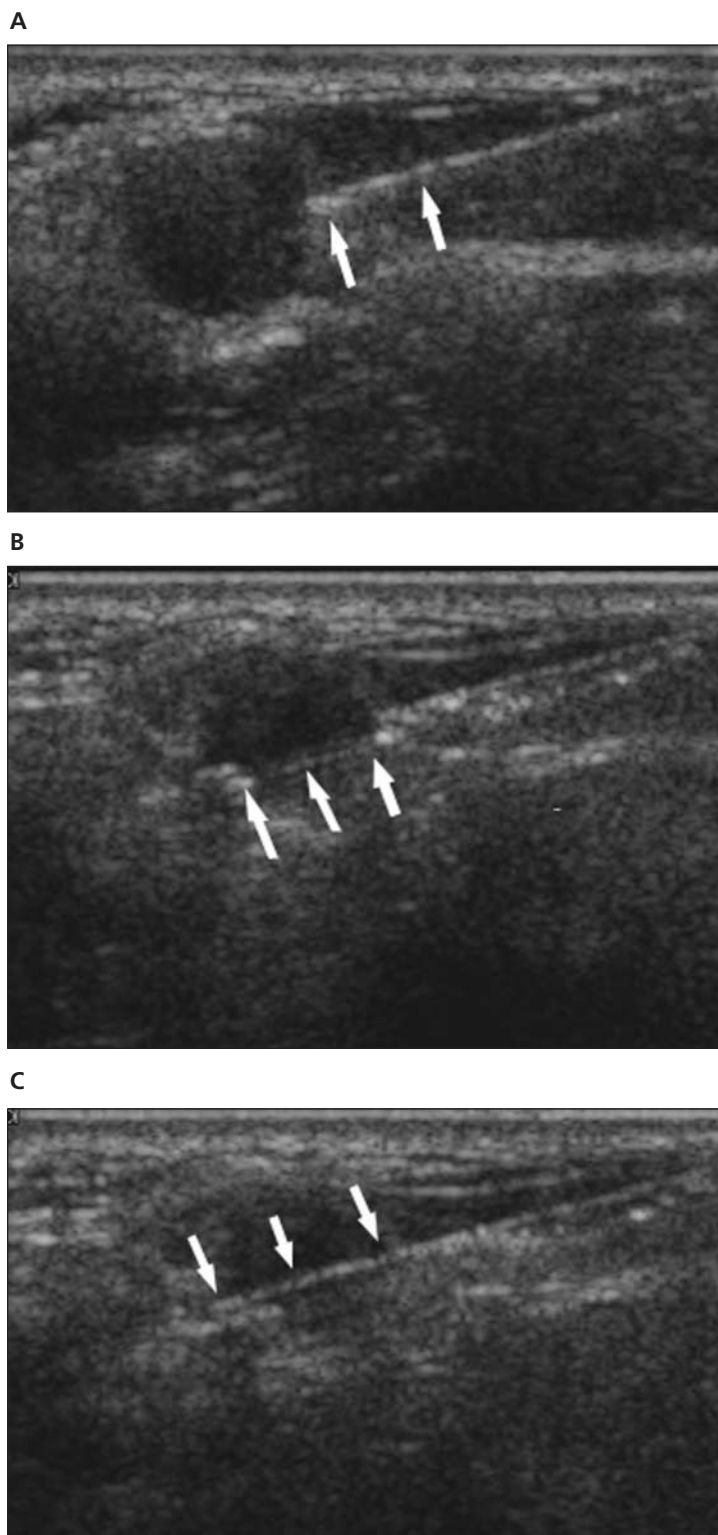


Table 1. Histologic Diagnoses of the Adequately Sampled Cases by Core Biopsy and Confirmed Diagnoses (n = 146)

Histologic Diagnosis (n)	Age, y, Range (Mean)	Confirmed Diagnosis (n [%])
Metastatic lymphadenopathy (16)	42–69 (51.6)	Metastatic lymphadenopathy (15 [94]), anaplastic large cell lymphoma (1 [6])
Non-Hodgkin lymphoma (12)	13–82 (56.6)	Non-Hodgkin lymphoma (12 [100])
Hodgkin lymphoma (4*)	13–58 (40.2)	Hodgkin lymphoma (4 [100])
Tuberculosis (37†)	22–70 (41.6)	Tuberculosis (37 [100])
Kikuchi disease (25)	16–43 (27)	Kikuchi disease (25 [100])
Toxoplasmosis (1)	44	Toxoplasmosis (1 [100])
Nonspecific reactive hyperplasia (44)	15–62 (35.8)	Reactive hyperplasia (44 [100])
Normal (7)	13–64 (37.1)	Normal (6 [86%]), toxoplasmosis (1 [14])

*One was highly suggested at core biopsy and was confirmed by subsequent excision biopsy.

†One of 37 cases was highly suggested at core biopsy and was confirmed by subsequent excision biopsy. Two of the total of 39 cases of tuberculous lymphadenitis showed nondiagnostic results at core biopsy.

specimen obtained by core biopsy was consistent with the primary tumor in 14 patients with metastatic lymphadenopathy. One patient who was reported as having metastatic lymphadenopathy was confirmed as having anaplastic large cell lymphoma at subsequent excision biopsy. In the other reported as metastatic neuroendocrine carcinoma at core biopsy, primary cancer could not be found despite a thorough workup, but subsequent excision biopsy revealed the same histologic diagnosis as neuroendocrine carcinoma.

An exact subclassification of the lymphoma by sonographically guided core biopsy could be made in all 12 patients with non-Hodgkin lymphoma and in 2 of 4 patients with Hodgkin lymphoma.

In 4 of 12 patients with non-Hodgkin lymphoma and in 3 of 4 patients with Hodgkin lymphoma, excision biopsies were performed and revealed histologic subclassifications identical to those by sonographically guided core biopsies. Table 3 summarizes the sensitivity, specificity, and accuracy of sonographically guided core needle biopsy in differentiating benign from malignant lymphadenopathy and in differentiating lymphoma from reactive hyperplasia.

Tuberculosis was definitively diagnosed by sonographically guided core biopsy in 36 (92.3%) of 39 patients. In 1 patient, a highly suggestive diagnosis of tuberculous lymphadenitis was reported and was confirmed by subsequent exci-

Table 2. Histologic Diagnoses of Malignant Lymphadenopathy by Sonographically Guided Core Biopsy and Confirmed Primary Cancer or Lymphoma at Excision Biopsy (n = 33)

Diagnosis at Core Needle Biopsy (n)	Confirmed Primary Cancer or Classification of Lymphoma at Excision Biopsy (n)
Squamous carcinoma (6)	Nasopharynx (4), lung (1), uterine cervix (1)
Poorly differentiated carcinoma (4)	Lung (2), tongue base (1), hepatoma (1)
Adenocarcinoma (1)	Uterine cervical adenocarcinoma (1)
Small cell carcinoma (1)	Small cell lung cancer (1)
Neuroendocrine carcinoma (1)	Primary cancer not found
Histiocytic sarcoma (1)	Distal ileal histiocytic sarcoma (1)
Melanoma (1)	Left finger melanoma (1)
Metastatic carcinoma (1)	Anaplastic large cell lymphoma (1)
Diffuse large B cell lymphoma (9)	Diffuse large B-cell lymphoma (2)
Burkitt lymphoma (1)	Burkitt lymphoma (1)
Anaplastic large cell lymphoma (1)	Anaplastic large cell lymphoma (1)
Precursor B cell lymphoma (1)	Precursor B-cell lymphoma (1)
Mantle cell lymphoma (1)	Mantle cell lymphoma (1)
Hodgkin lymphoma (4)	Hodgkin lymphoma (3)

All histologic diagnoses of primary cancer were identical to those at core biopsies of lymph nodes except for 2 cases. Primary cancer could not be found in 1 of those 2 cases, and anaplastic large cell lymphoma was confirmed at excision biopsy in the other.

Table 3. Sensitivity, Specificity, and Accuracy of Sonographically Guided Core Biopsy of Cervical Lymphadenopathy for Differentiating Benign From Malignant and Lymphoma From Nonspecific Reactive Hyperplasia

Analysis	Differentiation of Benign From Malignant Lymphadenopathy			Differentiation of Lymphoma From Nonspecific Reactive Hyperplasia		
	Sensitivity, %	Specificity, %	Accuracy, %	Sensitivity, %	Specificity, %	Accuracy, %
I (n = 155)*	NA	NA	93.5	NA	NA	86.7
II (n = 146)†	96.8	100	99.3	93.7	100	98.3

*All biopsies were included in the analysis. Nondiagnostic results and highly suggestive diagnoses were regarded as incorrect diagnoses. NA indicates not applicable: sensitivity and specificity could not be calculated from these data.

†Nondiagnostic results were excluded in the analysis, and suggestive diagnoses were regarded as incorrect diagnoses.

sion biopsy. Nondiagnostic results were reported in 2 patients with tuberculous lymphadenitis, which were confirmed as tuberculous lymphadenitis at subsequent excision biopsy. Kikuchi disease was definitely diagnosed by core biopsy in all 25 patients, among which 5 had the diagnosis confirmed by subsequent excision biopsy, and 20 had the diagnosis confirmed by clinical and sonographic follow-up for more than 12 months. Table 4 summarized the sensitivity, specificity, and accuracy of sonographically guided core biopsy for diagnosing the cause of cervical lymphadenopathy, regardless of benignity or malignancy.

There were no procedure-related immediate or delayed complications in any of the 155 patients.

Discussion

Fine-needle aspiration cytologic examination is a safe and efficient procedure for diagnosis of malignant cervical lymphadenopathy. However, it has some limitations, even when performed in optimum circumstances. It may be difficult to distinguish low-grade lymphoma from reactive hyperplasia, and the diagnosis of lymphoma is not considered definitive.⁹ It may provide a possible diagnosis and indicate the need for nodal

excision for formal histologic assessment of the entire nodal architecture.^{9,10} Fine-needle aspiration cytologic examination also has a relatively high rate of nondiagnostic results, which sometimes are reported only as “negative for malignancy” and which may be problematic in management of cervical lymphadenopathy because some benign diseases such as tuberculous lymphadenitis requires specific antibiotic treatment.

Sonographically guided core biopsy is a well-established technique that is widely used in the abdomen and breast.¹¹ The major potential complications of core biopsy are hemorrhage and tumor seeding, which are unusual with small-bore needles. Sonographically guided core needle biopsy was not associated with an increased incidence of local recurrence.^{11–13} A few series reported its routine use in the head and neck. This may be due to a reluctance to use an automated biopsy device in an anatomic site that contains numerous major vessels and nerves. The use of sonographic guidance enables us to accurately target the lesion and to avoid injury to major vessels and nerves, resulting in higher diagnostic accuracy and a lower complication rate. Reported rates of hematoma after sonographically guided core needle biopsy

Table 4. Sensitivity, Specificity, and Accuracy of Sonographically Guided Core Biopsy of Cervical Lymphadenopathy for Diagnosing the Cause of Cervical Lymphadenopathy

Analysis	Sensitivity, n (%)	Specificity, n (%)	Accuracy, n (%)
I (n = 155)*	NA	NA	143/155 (92.2)
II (n = 146)†	94/96 (97.9)	113/114 (99.1)	143/146 (97.9)

*All biopsies were included in the analysis. Nondiagnostic results and highly suggestive diagnoses were regarded as incorrect diagnoses. NA indicates not applicable: sensitivity and specificity could not be calculated from these data.

†Nondiagnostic results were excluded in the analysis, and suggestive diagnoses were regarded as incorrect diagnoses.

of neck lymph nodes ranged from 0% to 1.2% (0 of 82 patients to 3 minor hematomas in 247 patients).^{7,8} In our study, no postbiopsy hematoma was detected. The use of color Doppler sonography for detecting intervening vessels and careful sonographic guidance enabled us to prevent postbiopsy hematoma.

In this study, the results of sonographically guided core biopsy were better in differentiating benign causes from malignancy and in differentiating lymphoma from reactive hyperplasia than those of FNAC reported in literature.¹⁻⁵ In addition, accurate subclassification of the lymphoma was possible in all 12 patients with non-Hodgkin lymphoma and 2 of 4 patients with Hodgkin lymphoma. The results of this study were consistent with those in previous reports.^{7,8}

Among the benign causes of unexplained cervical lymphadenopathy, tuberculous lymphadenitis is important because timely and appropriate antituberculosis medication is essential for treatment. Therefore, prompt and accurate diagnosis is necessary for tuberculous lymphadenitis. It can be quite difficult to reliably diagnose tuberculous lymphadenitis by clinical assessment and imaging studies; therefore, cytopathologic, microbiological, or histologic diagnosis is imperative.¹⁴⁻¹⁶ The sensitivity and accuracy of FNAC are not very high for tuberculous lymphadenitis, mainly because of nondiagnostic sampling.^{15,17,18} In our study, the cases of tuberculous lymphadenitis were easily diagnosed by sonographically guided core biopsy. The patients with tuberculous lymphadenitis were appropriately treated without delay or additional excision biopsy.

Kikuchi disease usually presents with unexplained cervical lymphadenopathy and is generally known as a self-limiting disease. It is not rare in Asian populations. It is difficult to distinguish Kikuchi disease from lymphoma or tuberculous lymphadenitis clinically, and it is also difficult to differentiate Kikuchi disease from lymphoma, metastasis, or tuberculous lymphadenitis on the basis of imaging studies in some cases.¹⁹ Because FNAC also has low accuracy for Kikuchi disease, excision biopsy is frequently required.^{20,21} On core biopsy specimens, Kikuchi disease could be diagnosed on the basis of the following histologic findings: (1) paracortical necrosis, (2) fibrinoid necrosis, and (3) a mixture of variable propor-

tions of benign histiocytes. In this study, Kikuchi disease was definitely diagnosed in all 25 patients by sonographically guided core biopsy, which prevented most of the patients from undergoing unnecessary excision biopsy.

In this study, there were 9 cases of nondiagnostic core biopsy results, of which 7 were confirmed at subsequent excision biopsy. Among the 7 cases, 2 cases of tuberculous lymphadenitis were heavily calcified lymph nodes, which may have been the cause of the nondiagnostic results at core biopsy. One case of follicular lymphoma, which was very difficult to differentiate from reactive hyperplasia, was confirmed by excision biopsy. In the remaining 4 cases of reactive hyperplasia, we infer that it was difficult to differentiate it from low-grade lymphoma because of limited tissue samples.

This study had a potential limitation in that the clinical and sonographic follow-up results as well as the results of excision biopsy were used as final diagnoses. However, because all the lymph nodes with benign results at sonographically guided core biopsy that had not changed or had increased in size during the follow-up were confirmed by excision biopsy, and because the lymph nodes with benign results at sonographically guided core biopsy were regarded as benign when they regressed spontaneously or by appropriate management, it was considerably reliable that the diagnosis at sonographically guided core biopsy was considered correct.

In conclusion, the results of this study reveal a high yield and accuracy of sonographically guided core biopsy for both benign and malignant causes of cervical lymphadenopathy. Sonographically guided core biopsy is a safe and efficient procedure for diagnosing the cause of cervical lymphadenopathy and may obviate unnecessary excision biopsy.

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